

ABSTRACTS

(This section of the JOURNAL is published in collaboration with the two abstracting journals, *Abstracts of World Medicine*, and *Abstracts of World Surgery, Obstetrics, and Gynaecology*, published by the British Medical Association. The abstracts are divided into the following sections: syphilis, (general, therapeutic, pathology); gonorrhœa (general, therapeutic, pathology); other venereal disease conditions; public health. After each subsection of abstracts follows a list of articles that have been noted but not abstracted. All subsections will not necessarily be represented in each issue.)

SYPHILIS (Therapeutic)

Reactions to Twenty-day Intensive Therapy with Mapharsen and Bismuth for Syphilis with a Note on the Use of Bal in their Management. CORMIA, F. E. U., and BLAUNER, S. G. (1947). *Amer. J. Syph.*, 31, 135.

Five hundred patients, of whom 185 had serum-negative and 164 serum-positive primary syphilis, 89 secondary syphilis, 60 latent syphilis, and 2 asymptomatic neurosyphilis, were treated by the 20-day intensive schedule with 1 mg. "mapharsen" per kilo body weight daily (maximum daily 75 mg.) and 0.2 g. of bismuth subsalicylate every 3 days to a total of eight injections.

In the first 300 patients the blood count was taken and the non-protein nitrogen was estimated on admission and weekly thereafter. White-cell counts were taken in the middle of each week; the icterus index was determined, the urine examined, and the Rumpel-Leede tourniquet test performed every 3 days. Temperature records gave the most valuable evidence of toxicity. In the remainder of the patients the number of white cells and the non-protein nitrogen were estimated on admission and on discharge, and the icterus index was determined and the urine examined weekly.

Treatment of 476 patients was complete and of 24 incomplete. Of these last, 7 had cerebral irritation, 6 jaundice, 3 toxic erythema, 3 agranulocytosis, 2 severe fever, 2 hæmorrhagic encephalitis, and 1 persistent albuminuria. Reactions in 190 (37.6%) were sufficiently severe to cause modification of the schedule; of these, 125 had fever, 33 toxic erythema, 14 cerebral irritation, 6 jaundice, 3 agranulocytosis, and 2 hæmorrhagic encephalitis. The majority of reactions appeared before the tenth day, were more often seen in primary syphilis, and appeared unrelated to previous Herxheimer reactions.

When treatment was resumed smaller doses of from one-fifth to one-half the previous dose, increasing to the maximum in from 2 to 5 days, were given in the mild cases; more severe cases received 1/100 of the dose, increasing to the maximum in 7 days. On resumption there was increased liability to both toxic erythema and

fever. A previous attack of fever had occurred in the cases of jaundice and agranulocytosis, and, though such an event was exceptional in those patients showing cerebral irritation and encephalitis, fever was usually noted as a prodromal or concurrent sign. Seventeen patients—4 with fever, 3 with toxic erythema, 8 with cerebral irritation, and 2 with agranulocytosis—received 2,3-dimercaptopropanol (BAL) by injection with apparently good results. One patient with hæmorrhagic encephalitis was given this drug by inunction with no demonstrable benefit.

The late onset of stomatitis probably prevented many cases with complications due to bismuth from being seen, but 5 severe cases were noted. There were also 2 instances of bismuth dermatitis, 5 of bismuth arthralgia, and 3 of bismuth "grippe." Four patients had albuminuria at the start, and in 2 of these bismuth was discontinued as this was increasing. In no case did albuminuria arise *de novo* during the course.

R. R. Willcox

Six to Twelve Month Follow-up Results in Early Syphilis Treated by a Twenty-day Intensive Arseno-bismuth System. PILLSBURY, D. M., and LOVEMAN, A. B. (1947). *Amer. J. Syph.*, 31, 115.

The results are reported of a follow-up lasting 6 months of 982 male patients treated for early syphilis by the "20-day" arsenic and bismuth regime (arsenoxide 20 mg. per kilo body weight, divided into twenty daily doses, with eight injections, each of 0.2 g., of bismuth salicylate). Though the treatment was toxic there were no deaths, and of the first 775 patients 96.3% completed the course. Two facts are outstanding—serious reactions rarely occur during the first 5 days, and when they do they are almost invariably ushered in by fever. Of the 982 patients observed for 6 months, those with serum-negative primary syphilis gave 98.68% of negative serum reactions, those with serum-positive primary syphilis 95.1%, those with secondary syphilis 92.68%, and those with latent syphilis 76.32%; at 12 months in 258 cases the respective percentages for the first three groups were 97.56, 93.4, and 95.45. Approximately twice

as many unsatisfactory results were noted after 12 months as after 6 [a point of some importance as regards ultimate prognosis]. Serological relapses, excluding the latent cases, were commonest in the secondary group at 6 months (2.44%), but in the serum-positive primary group at 12 months (5.66%). The cerebrospinal fluid of 785 patients was examined 6 or more months after treatment, and 6 (0.76%) were found positive. It is concluded that though the results are satisfactory this method of treatment is unjustifiable when penicillin is available. *T. E. Osmond*

The Treatment of Early Syphilis by the Twenty-six-week Mapharsen-bismuth Schedule. STERNBERG, T. H., and LEIFER, W. (1947). *Amer. J. Syph.*, 31, 124.

The "26-week" schedule for the treatment of early syphilis was adopted in the American Army early in 1942; it consisted of 40 injections of "mapharsen" (total 2.4 g.) and 16 injections of bismuth (total 3.2 g.) over a period of 26 weeks. The present article analyses the results in 3,000 patients, of whom 1,330 were in the serum-negative primary, 1,207 in the serum-positive primary, and 463 in the secondary stage. Toxic reactions occurred in 63 patients and were mostly gastro-intestinal or pyrexial; there were no deaths; and in only 2 cases, 1 of jaundice and 1 of dermatitis, was it necessary to abandon arsenical therapy. (It is estimated that the expected mortality rate from this treatment is about 1 in 33,000 cases.) Patients were kept under observation for varying periods up to 3 years, the majority for 12 to 18 months. Serum-negative primary cases showed 98.25% "satisfactory" results; serum-positive primary 94.48% and secondary 84.34%. In the whole series only 18 (0.64%) showed pathological changes in the cerebrospinal fluid; of these, 4 were in group I, 4 in group II, and 10 in group III. Of these tests, 91.1% were carried out during the first 24 months of observation. It is emphasized that the results do not represent the cure rate; with longer observations there might have been more relapses, though, on the other hand, many persistently positive sera might have reverted to negative. *T. E. Osmond*

Rapid Treatment of Prenatal Syphilis. OLANSKY, S., and BECK, R. (1947). *Amer. J. Syph.*, 31, 51.

Although congenital syphilis can be prevented, thousands of infected infants are born in the United States each year. The authors conclude that many syphilitic women do not receive adequate treatment during pregnancy, and believe this failure to be due to the fact that standard methods of antisiphilitic treatment take too long and are too difficult for the average patient. [In Britain congenital syphilis usually follows failure to diagnose maternal syphilis; the known syphilitic mother is usually co-operative, and attends well for treatment throughout her pregnancy.] The authors have therefore studied intensive-treatment methods in an attempt to prevent prenatal syphilis,

and here report the results in 147 patients, of whom 129 were studied for 3 months or longer after confinement. There were 128 live births, 5 abortions, and 6 stillbirths. The 128 live infants were free from clinical signs of syphilis, and only 1 had persistently positive serological evidence. In 2 cases of stillbirth the foetus showed no pathological evidence of syphilis, and in another 2 it was considered that the foetus had died before treatment was started. One of the abortions was considered to be traumatic, and in another the foetus was thought to be dead before treatment was started.

The treatment schedules used were: (1) 1,200 mg. "mapharsen" by slow intravenous drip over 5 or 8 days combined with 0.2 g. bismuth subsalicylate weekly for 8 weeks; (2) 60 injections of 40,000 units of penicillin at 3-hourly intervals; (3) (a) 1 mg. mapharsen per kilo body weight (maximum of 60 mg. per dose) daily for 8 injections, 10,000 units of penicillin every 3 hours for 60 injections, and 0.2 g. bismuth subsalicylate on the first, fifth, and ninth days; (3) (b) injections of mapharsen on the first, third, fifth, seventh, and ninth days, 16,667 units of penicillin intramuscularly every 3 hours for 72 injections, and 3 injections of 0.2 g. bismuth subsalicylate. The findings justify the authors' conclusion that intensive antisiphilitic treatment even late in pregnancy results in a high proportion of non-syphilitic infants. *S. M. Laird*

The Relative Toxicity and Therapeutic Activity in Experimental Syphilis of Bismuth Subsalicylate, Bismosol, and Biliposol. EAGLE, H. (1946). *Amer. J. Syph.*, 30, 549.

Three preparations, representative of the water-soluble, the fat-soluble, and the insoluble types of bismuth compounds, were used for this investigation. The author considers the bismuth preparations as a group to be from one-half to one-third as active as "mapharsen"; and the safety zone between the effective and toxic doses to be from six to eight times greater than that provided by mapharsen. *V. E. Lloyd*

The Rapid Treatment of Syphilis: Comparison of Results Using Five Treatment Methods. LEAVITT, H. M. (1947). *Amer. J. Syph.*, 31, 27.

After treatment in hospital with one of five different methods, 539 patients with syphilis were followed up for 6 or more months. The five treatment schedules were: (1) A daily injection of "mapharsen" (usually 0.06 g.) for 6 days a week for twenty doses, together with a weekly injection of 0.2 g. bismuth subsalicylate. A further 8 weekly injections of bismuth after the patient left hospital were advised. (2) Daily injections of mapharsen 6 days a week up to a total of twenty-two injections; injection of 0.2 g. bismuth subsalicylate on the first day of treatment and with every fifth injection of mapharsen. (3) Sixty injections of 40,000 units of penicillin at 3-hourly intervals (total 2,400,000 units in 7½ days). (4) A combined treatment—the "8-6-3" schedule—lasting 8 days comprising eight daily injections of mapharsen,

three injections of bismuth subsalicylate, and 10,000 units of penicillin 3-hourly for sixty injections (total 600,000). (5) A modification of (4), the "5-12-3" schedule, consisting of five injections of mapharsen in 9 days, three injections of bismuth subsalicylate, and seventy-two injections of 16,667 units of penicillin at 3-hourly intervals (total 1,200,000).

It was found that none of these five schedules was superior to long-term therapy or intensive arsenotherapy. Penicillin alone (3) was the safest, while the "8-6-3" schedule (4) produced two severe but non-fatal cases of arsenical encephalopathy. Further work is needed to determine the optimum combination of penicillin, arsenic, and bismuth required for the effective treatment of syphilis in its various stages.

[While the results are disappointing, they do indicate that the optimum treatment required must be more than that given in the schedules.]

S. M. Laird

Injury to the Hæmopoietic System during Arsenotherapy for Syphilis Complicated by Diphtheria. (Beschadiging van de bloedbereidende organen tijdens arseno-benzolbehandeling van lues, welke door diphtherie is gecompliceerd.) HOHMANN, W. J. (1946). *Ned. Tijdschr. Geneesk.*, 90, 1562.

After giving two case histories (one fatal) the author points to the danger of treating syphilis with heavy metals during or shortly after an attack of diphtheria, and recommends replacing them in such cases by penicillin.

R. Salm

Dichlorophenarsine Hydrochloride in the Treatment of Syphilis. BEERMAN, H., and WAMMOCK, V. S. (1947). *Amer. J. Syph.*, 31, 150.

Dichlorophenarsine hydrochloride is an almost colourless powder first described by the Germans in 1914. It is readily soluble in water, being converted into the arsenoxide and forming a yellowish solution which darkens on oxidation. The maximum standard dose is 0.068 g. for males and 0.045 g. for females. Early trials showed it to be ineffective in human syphilis, but success has since been obtained with buffered solutions and it is manufactured commercially as "chlor-arsen."

In the present study 521 patients received from one to forty injections each (total 8,575) of a preparation of dichlorophenarsine hydrochloride buffered with four parts of sodium ascorbate. Sixty-two had primary, 116 secondary, and 343 later forms of syphilis. Three treatment schedules were used. To 310 patients the routine treatment was given; this consisted of continuous alternating courses of weekly injections of 0.03 to 0.068 g. of the drug combined with 0.26 g. of bismuth subsalicylate to a total of thirty arsenical and sixty bismuth injections. The doses and the duration of treatment in this schedule were increased by about one-quarter for the latter forms of syphilis. The so-called 26-week Army course was used for 189 patients and the Eagle and Hogan 12-week modified intensive course was employed for 22 patients.

Spirochaetes disappeared as quickly, healing of lesions was as satisfactory, and serological reversal was as rapid as with "mapharsen." There were only 3 cases of serological and no case of infectious relapse. The total absence of the latter is attributed to the incomplete follow-up, information in respect of 206 of the 521 patients being for periods under 6 months.

Seventy-one patients (13.6%) had mild reactions: 52 had nausea and vomiting, 2 nausea and diarrhoea, 1 chills and abdominal pain, 1 abdominal pain alone, 2 dizziness, 4 headache, 2 chills and fever, and 1 each pain in the back, rash, and nitritoid crisis. [The remainder are not listed.] Three had Herxheimer reactions. Thirty-eight patients were later given the drug without adjuvants and there was no reaction; 6 more received the drug with benzocaine lozenges and 8 with atropine before injection; there were no reactions. While some patients intolerant of the drug subsequently received neoarsphenamine without reaction, 11 patients previously showing reactions to neoarsphenamine tolerated dichlorophenarsine hydrochloride. It is concluded that the drug is a safe and effective arsenical suitable for use instead of mapharsen.

R. R. Willcox

Penicillin in the Treatment of Experimental Syphilis of Rabbits. I. The Therapeutic Activity of Penicillin in Single and Multiple Doses in Isotonic Solution of Sodium Chloride and Peanut Oil-Beeswax by Intramuscular Injection. KOLMER, J. A. (1947). *Arch. Derm. Syph.*, Chicago, 55, 741.

Rabbit experiments were performed with two specimens of penicillin of a potency of 544 and 1,624 units per mg., and of a G content of 88 and 92% respectively. These penicillins, dissolved in isotonic saline solution, were compared in their effect on rabbit syphilis with the same penicillins suspended in a mixture of arachis oil and 3% beeswax at a concentration of 10,000 units per ml. All rabbits were inoculated intratesticularly with the Nichols strain of *Treponema pallidum* and all developed orchitis positive on dark-field examination 5 to 6 weeks later. Treatment was then instituted and dark-field examinations performed daily for 3 days and thereafter weekly for 10 weeks; at the end of this time the popliteal lymph-nodes were inoculated into the testicles of fresh animals and these were observed for a minimum of 4 months.

Two rabbits were each given single injections of both penicillins in saline solution in doses of 10,000, 30,000, and 100,000 units per kilo body weight. Though preliminary dark-field tests became negative, all 12 rabbits later relapsed and showed positive lymph node transfers. With the same doses of penicillin in oil-wax, however, a cure was obtained in 3 out of 4 receiving a single injection of 10,000 units per kilo and in all 8 receiving the larger amounts.

When injections were given daily multiple doses of 1,000, 5,000, and 25,000 units per kilo were employed once daily for 8 days. With saline solution, temporary improvement with later

relapse was noted in all 4 on the lowest-dose and in 3 with the total dose of 40,000 units; no improvement was noted with the total dose of 200,000 units. With penicillin in oil-beeswax 3 out of 4 rabbits were cured by the lowest dose and all by greater doses. With multiple injections of the same doses given twice daily over 8 days, 3 out of 4 rabbits responded to the lowest doses of saline solution and all to the higher doses, while with penicillin in oil-beeswax all 12 animals were cured.

Thus the results with penicillin in oil-beeswax in rabbit syphilis show a decided improvement on those with penicillin in saline solution.

R. R. Willcox

Relation of the Size of the Inoculum and the Age of the Infection to the Curative Dose of Penicillin in Experimental Syphilis, with Particular Reference to the Feasibility of its Prophylactic Use. EAGLE, H., MAGNUSON, H. J., and FLEISCHMAN, R. (1947). *J. exp. Med.*, 75, 423.

Material used in this study consisted of the Nichols strain of *Treponema pallidum* passaged intratesticularly. Inocula were obtained by emulsification of rabbit testicular chancre in 50% rabbit serum and dilution to obtain concentrations of 10^4 , 10^4 , and 10^4 , organisms per ml., 0.2 ml. of the appropriate dilution being injected intracutaneously or intratesticularly. Penicillin, in one single intramuscular dose of a suspension in oil and beeswax, was administered 4 hours, 4 days, or 2 weeks after inoculation. At each of these intervals groups of 4 to 11 rabbits were given increasing doses to determine the abortive dose of penicillin required. This latter dose was compared with that necessary to cure animals treated 6 weeks after inoculation and after a lesion had developed. Administration of relatively small doses of penicillin 4 days after inoculation aborted the disease; the preventive dose (PD) varied with the size of inoculum and with the age of the infection. Thus, in animals inoculated with 20, 2,000, and 200,000 spirochaetes and treated 4 days later, 200, 500, and 3,500 units per kilo, respectively, were needed to protect half the animals, and the corresponding PD90 dosages were 500, 2,000, and 16,000 units per kilo. With a fixed intratesticular inoculum the PD50 of penicillin remained at a constant level for 4 days. By the end of the second week more than seven times the dosage was required, while by the sixth week, after the appearance of the chancre, more than thirty times the amount was necessary to produce the same results.

The authors consider that administration of penicillin in one single intramuscular dose shortly after contact might prove a successful form of prophylaxis in human infection. In man and rabbit renal clearance of penicillins F, G, and X is maximal, the blood level falls at essentially the same rate, and after intramuscular inoculation there are comparable rates of absorption. Equal dosages per kilo in both species should, therefore, produce similar results on the spirochæte. Thus,

in the average adult, a single intramuscular injection of 15,000 units in peanut oil and beeswax after, say, 4 days' exposure might effectively abort infection. Even oral administration of three to five times this dose should prove effective. This suggests a new approach to the prophylaxis of syphilis, for if the spirochæte multiplies as slowly in man as it does in the rabbit a single dose of penicillin, orally or intramuscularly, should even abort the infection if it is given days after exposure.

M. M. Buchanan

Effect of Penicillin on Serology of Late and Latent Syphilis. (A Study of 120 Cases Followed for Six Months or More.) WILLCOX, R. R. (1947). *Lancet*, 2, 8.

The author studied the effect of penicillin on the serology of 120 military personnel treated at an army hospital for congenital, latent, and late syphilis. The comparatively short time of 6 months' observation or more was sufficient to detect the trend of the early pathological changes in response to penicillin. A qualitative Wassermann and a quantitative Kahn test were carried out on the blood serum once a month for the first 6 months, quarterly for the following year, and 6-monthly for a further year. The cerebrospinal fluid was examined before penicillin was given and again after 6 months. It will again be examined after 2 years.

The cases were divided into four clinical groups: congenital syphilis, 25; early latent syphilis (known infection within 5 years), 33; latent syphilis (duration unknown), 34; and late symptomatic syphilis, 28. Serological results are ingeniously arranged into four groups of varying stability: (1) low declining titre, (2) high fluctuating titre, (3) high fixed titre (completely resistant to previous treatment), and (4) high titre of unknown stability (not previously treated). Groups 1 and 2, both with fluctuating titres after previous treatment, responded most favourably (74.2 and 94.4%), while group 3, with fixed titre to arsenic and bismuth, gave little evidence of further improvement (16.1%). Group 4, a mixture of the other groups, showed indifferent success (27.5%). The results in cases with an initially low titre were better after 6 months but the improvement was not maintained and an appreciable number of patients relapsed. The improvement continued for 9 or 12 months in the cases with a high fluctuating titre. Latent syphilis of recent origin responded most, while late syphilis and congenital syphilis responded least. The cerebrospinal fluid was abnormal in 18 cases; only 9 cases had improved of the 15 examined 6 months later, and only 3 among the 9 showed similar improvement in the blood. In this small series the findings in the blood and in the cerebrospinal fluid were not parallel.

As the author states, the analysis is confused because many patients had been treated with arsenic and bismuth before penicillin was given. Again, some patients were given arsenic and bismuth after penicillin; failure in these cases, however, would imply failure after penicillin alone.

Patients had a total dosage of 2,400,000, 4,000,000, and 4,800,000 units of commercial penicillin in aqueous solution in 3-hourly injections of 40,000 units. Six of the 25 congenital syphilitic patients improved. All the 33 cases with early latent syphilis had had arsenic and bismuth previously; 26 (78.8%) improved. As would be expected, results were less satisfactory in patients with latent syphilis of unknown duration: 16 out of 34 responded. At the end of 6 months only 8 (28.6%) of the 28 patients with late, mostly gummatous, syphilis had improved.

[The marked difference in the total dosage of penicillin in the three schedules of treatment must affect the value of the comparative figures in this study; accurate comparisons can hardly be made, since the dosage received by the various categories of patients is omitted.]

T. Anwyl-Davies

The Clinical, Radiologic, and Pathologic Aspects of Late Pulmonary Syphilis—Effects of Penicillin Therapy. KULCHAR, G. V., and WINDHOLZ, F. (1947). *Amer. J. Syph.*, 31, 166.

Four cases are described of the extremely rare late pulmonary manifestations of syphilis, 1 of which was treated successfully with penicillin. Necropsy figures as to incidence have varied from 1 in 3,000 to 12 in 1,500. It is suggested that late pulmonary syphilis may be more common than is realized. Recorded cases have shown it to be nearly twice as common in males as females and to have an age incidence between 2 and 98 years. Most cases were diagnosed 5 or more years after infection (10 to 11 years was not uncommon). It is not infrequently associated with cardiovascular syphilis, and some workers have suggested that the pulmonary process is an extension of earlier disease in the mediastinum.

The disease may be asymptomatic or may appear as a chronic chest lesion with chronic cough and sputum, sometimes blood-stained, associated with dyspnoea, loss of weight, and sometimes night sweats, pain in the chest, and even severe hæmoptysis. Before syphilis of the lung can be diagnosed the commoner pulmonary lesions of pneumonia, neoplasm, fungus infections, and tuberculosis must be excluded, and a history of previous syphilis (if possible) and a positive serological reaction obtained. The lesion should show clinical and radiological improvement with antisyphilitic treatment. The disease may occur as an acute syphilitic bronchopneumonia, a chronic interstitial syphilitic pneumonia, a syphilitic bronchiectasis, or a gumma. From the clinical standpoint no differentiation of these types is possible. The radiological appearances are not specific, though rounded shadows like tumour masses are sometimes seen in the lower lung fields and, if interstitial fibrosis predominates, radiating parenchymal markings are observed in the hilar region. The condition should be considered whenever bizarre lung films are seen. It is very rare for *Treponema pallidum* to be recovered from the lesions.

In the first case described a white man aged 73, had had a penile sore at the age of 21. He was admitted to hospital with syphilitic aortitis, and

radiographs showed involvement of the right lower lung field. The second patient, a woman aged 56 with a gumma of the neck, had no symptoms but a hilar shadow which disappeared after antisyphilitic treatment. In the third case, that of a man of 33 years, a hilar shadow was also seen in the radiograph. Treatment was purposely withheld for 3 months, no change being observed; the lesion subsequently resolved under treatment. In the fourth patient, a man of 29, there was a strongly positive serological reaction associated with periostitis of the left femur and the first left metacarpal bone; a radiograph showed a sharply outlined rounded density 1 in. in diameter in the sub-pleural region of the left lower lobe. After 2,400,000 units of penicillin had been administered (40,000 units every 3 hours for 7½ days) the radiological findings became almost normal within a month and remained so 5 months later.

R. R. Willcox

Penicillin in the Treatment of Neurosyphilis. A Study of One Hundred Cases Followed Twelve Months or More. ROSE, A. S., and SOLOMON, H. C. (1947). *J. Amer. med. Ass.*, 133, 5.

The authors treated 236 neurosyphilitic patients with 3,000,000 units of penicillin between Feb. 1944, and April, 1946, and report the results in 100 who have been followed for a year or more. When fever therapy was also used the amount was about half that usually administered. The following are some of the results obtained: Penicillin plus malaria caused "improvement" in 66% of patients; penicillin fever with cabinet, 52%; and penicillin alone, 58%. Of the 100 patients 36 required re-treatment; it made little difference whether the penicillin was given 2-, 3-, or 4-hourly or whether it extended over 5, 7½, 10, or 15 days, though the authors state that the 15-day patients less often required re-treatment. Of 75 patients with general paralysis of the insane treated by one or other of the three methods, 69% were improved and 38% required re-treatment. As regards the spinal fluid, the cells tended to return to normal in 3 to 6 months, the protein in 6 to 9 months, and the Wassermann reaction more slowly, only 11 patients giving negative reactions. There were 12 deaths among the 236 patients, 6 of which were due to G.P.I. and the rest to causes other than syphilis; in 1 case of G.P.I. it was thought that penicillin contributed to the fatal result. It is concluded that the amount of treatment employed was inadequate for late symptomatic syphilis, and the amount of penicillin has now been doubled.

[The Wassermann reaction is stated to have been "carried out in six dilutions of spinal fluid as follows: 0.1, 0.2, 0.4, 0.6, 0.8, and 1.0 c.cm." These are not dilutions but absolute quantities.]

T. E. Osmond

Sulphonamide Therapy and Serological Reactions of Syphilis. (Terapia sulfamidica e reazioni sierologiche della lue.) RENATO, R. (1947). *G. Batt. Immun.*, 36, 3.

The question of false positive serological reactions after sulphonamide therapy was investi-

gated in 76 patients suffering from a variety of general medical, skin, and gonococcal affections. So far as could be determined, they had not had syphilis, and serological reactions were negative in all before treatment. The patients received sulphanilamide, sulphapyridine, sulphathiazole, or methyl-sulphathiazole, usually by mouth. The four serological reactions (Wassermann, Kahn, Meinicke, Sachs-Witebsky), repeated from 2 to 10 days after beginning treatment, became positive in 16 patients who had received from 12 to 90 g. of sulphonamide. In 2 patients the reactions remained slightly positive 2 months after stopping sulphonamide therapy but later reverted to normal; in the other 14 patients the reactions became negative after 10 days to 2 months. The flocculation reactions were more often positive than the Wassermann reaction, and all positive reactions were usually weak. After the serological reactions had returned to normal, provocative doses of bismuth and arsenobenzene were given, with negative results in all cases.

The author discusses the theoretical significance of these observations, particularly in relation to a possible disturbance of liver function by sulphonamide therapy, producing changes in serum proteins. The false positive reactions are weak and transient and should give rise to no diagnostic difficulty provided the tests are repeated when found positive in patients who have recently received sulphonamide therapy.

L. P. R. Fourman

SYPHILIS (Pathology)

The Antigenic Specificity of Syphilitic Antibody Globulin. HENRIKSEN, S. D. (1947). *J. Immunol.*, 55, 153.

The author reports investigations designed to study the immunizing properties of syphilitic antibody when injected into animals, and to compare the reactions of the immune sera thus produced to the homologous antigen and to various normal serum proteins.

Strongly positive syphilitic serum was flocculated with the antigen as described by Wadsworth and Brown (*J. Immunol.*, 1936, 31, 155), 0.5 to 1 volume of antigen per volume of inactivated serum proving experimentally to be the maximal flocculating dose; the floccules were centrifuged and washed four times with 10 to 15 ml. quantities of saline. The resulting dense suspensions of washed floccules were used for immunization. Rabbits were injected intravenously 2 to 3 times weekly for 3 to 4 weeks and bled 1 week after the last injection. Complement-fixation and precipitation tests were performed before and after absorption with the following antigens: strongly positive inactivated syphilitic serum; pooled inactivated normal serum; Wassermann antigen prepared by Kolmer's method; serum globulin and serum albumin; water-insoluble and water-soluble globulins; and purified syphilitic antibody.

The results showed that when such washed floccules are injected into rabbits two different antibodies are produced which can be differentiated from each other by absorption. One is directed

against the lipid antigens of the heart extract and is of a similar specificity to the syphilitic antibody, and the other is directed against the syphilitic antibody which is combined with the lipid antigen in the floccules. The specificity of the latter antibody is not characteristic of the specific reactive groupings of the exciting antigen, as it reacts just as well with normal human serum as with strongly Wassermann-positive serum. A comparison of the reactivity of the various protein fractions with the immune serum showed that practically all the reactive antigenic material is present in the globulin fraction. Within this fraction the reactive antigen was mainly concentrated in the water-insoluble portion. The author concludes that the specificity of the syphilitic antibody appears to be the same as that of certain normal serum globulins. The syphilitic antibody seems to be more closely related to the euglobulin than to the pseudoglobulin fraction.

A. Henderson-Begg

Experimental Syphilis. Qualitative and Quantitative Studies of Reagin in Normal and Syphilitic Rabbits. SHERWOOD, N. P., and COLLINS, C. (1946). *Amer. J. Syph.*, 30, 571.

The standard and quantitative Kahn, Kolmer, and Kline tests, and the differential temperature technique were employed in this inquiry. A group of 23 rabbits served as a control. The second group, studied as normals for some weeks, were then inoculated intratesticularly with *Treponema pallidum*, and all were tested at weekly intervals for from 7 to 51 weeks. All 23 normal rabbits showed some type of immune body at one time or another: the titre of the immune body was low and variable. The 52 inoculated animals were observed for periods of up to 51 weeks. Only 2 showed the general biological type of reaction throughout. The remainder showed various combinations of two or all three types of antigen. No correlation was found between their titre and type of immune body present in syphilitic rabbits. The differential temperature Kahn verification test did not show a quantitative difference between the immune body of normal and of syphilitic animals.

V. E. Lloyd

Transmission of Experimental Syphilis from Mouse to Mouse—Absence of *Spirochaeta pallida* and of Pathologic Changes in Presence of Successful Inoculation. WILE, U. J. (1947). *Amer. J. Syph.*, 31, 109.

The testicles of rabbits infected with the Nichols strain of *S. pallida* were ground up and injected into the brain and peritoneal cavity of mice; brain and organ emulsions of the mice infected a rabbit after 60 days. After a second, third, and fourth mouse passage the organs but not the brains were found to be infective; a fifth passage was attempted, but the rabbit showed no clinical evidence of syphilis though it developed a Kahn reaction of 80 units and proved resistant to inoculation at a later date. The intervals of time between inoculation of the rabbits with mouse material and the development of syphilitic lesions

were 27, 58, 48, and 81 days respectively, suggesting that the spirochaetes tended to diminish in virulence with successive transfers. In none of the mouse organs could spirochaetes be demonstrated by dark-ground examination, staining with hæmatoxylin-eosin, or the Warthin-Starry silver impregnation method. This suggests that the spirochaetes in the mice had assumed an infra-visible or granular form. It is interesting to note that the organs (spleens and gonads) of the mice were capable of carrying the infection much longer than the brains.

T. E. Osmond

False Positive Tests for Syphilis. A Study of their Incidence in Sporozoite-induced Vivax Malaria. REIN, C. R., and KENT, J. F. (1947). *J. Amer. med. Ass.*, 133, 1001.

Ninety male volunteers with no evidence of syphilis were inoculated by mosquito bite with sporozoites of vivax malaria. Specimens of serum were obtained from each patient before inoculation, at daily intervals during attacks, two or three times weekly after attacks, and at minimal weekly intervals for a total period of 18 months. The specimens were subjected to several tests for syphilis, including the standard Kahn, the Hinton flocculation, the Kline diagnostic and the Kline exclusion, the Mazzini and the Boerner-Jones-Lukens micro-flocculation tests, and a newly developed micro-flocculation test with a cardiolipin antigen (Rein and Bossak); 44,958 tests were carried out on a total of 7,493 sera.

Of the 90 patients, 57% developed false-positive reactions with one or more tests, but the Hinton gave only doubtful reactions over a 2-day period, and Rein and Bossak's remained negative throughout. The standard Kahn and Kline exclusion tests gave the strongest non-specific reactions. Most of the sera were subjected to several complement fixation tests including the Kolmer-Wassermann. About the same number of false-positive reactions were obtained as with the more usual flocculation tests.

G. L. M. McElligott

The Weltmann Serum Coagulation Reaction in Syphilis. CALLAWAY, J. L. (1947). *Amer. J. Syph.*, 31, 216.

The Weltmann serum coagulation reaction is a non-specific empirical test, comparable with the erythrocyte sedimentation rate, giving consistent values in the healthy and a definite range of deviation in certain pathological states such as acute infections. It is apparently unaffected by dehydration, acidosis, alkalosis, anæmia, or allergic states, and, while it bears no relation to the albumin-globulin ratio, there is a lower reading when the α -globulin level is high and vice versa.

The test is performed by mixing in ten tubes 0.05 ml. of the blood serum to be tested with 2.5 ml. of serial dilutions of from 0.1 to 0.01 ml. of 10% calcium chloride solution. The tubes are placed in a boiling water bath for 15 minutes before the number of tubes in which coagulation has occurred is ascertained. The normal is six, and a shift to the left is said to have occurred if

less, and to the right if more, are involved. Generally speaking, inflammations and infections cause a shift to the left, and fibrosis and degenerations to the right.

The serum of 610 syphilitic persons was examined; 132 had primary, 148 secondary, 162 latent, 34 congenital, and 21 cardiovascular syphilis, while 113 had neurosyphilis. The average readings for all groups but two were in the range 7.0 to 7.4; the reading for neurosyphilis was 6.3 and for prenatal syphilis 5.7. Of patients with early syphilis, 32 showed no appreciable change in the reaction after treatment for 6 months with arsenic and bismuth, as did 18 of the cases of neurosyphilis treated with fever, and 40 given penicillin. It is concluded that while a slight shift to the right can be observed in all forms of syphilis except congenital, the reaction is non-specific.

R. R. Willcox

GONORRHOEA (Therapeutic)

Arthritis in the Mediterranean Theatre of Operations. III. Clinical Description of Infectious and Other Types of Arthritis. SHORT, C. L. (1947). *New Engl. J. Med.*, 236, 468.

Infective types of joint disease in the Mediterranean theatre are reviewed. At the Twelfth General Hospital 20 out of 173 cases of dysentery developed arthritis, and of these 10 also developed urethritis or conjunctivitis or both (Reiter's syndrome). The author suggests that the dysentery merely provided a portal of entry for the causative agent of Reiter's syndrome, and he even regards the arthritis following dysentery as due to a secondary invader. He finds support for this view in the fact that neither the arthritis nor the urethritis reacts to chemotherapy, to which dysentery reacts readily.

Gonococcal arthritis was treated by sulphathiazole combined with intra-articular penicillin. Cases which failed to respond to this treatment are regarded as being cases of rheumatoid arthritis rather than of true gonococcal arthritis. Meningococcal arthritis was found to be little affected by chemotherapy or penicillin, but all cases recovered.

H. F. Turney

OTHER VENEREAL DISEASE CONDITIONS

Rickettsial Forms in Pus from Lymphogranuloma Venereum. (Sul reperto di forme Rickettsiose nel pus poradenitico.) D'IGNAZIO, C., and CODELEONCINI, E. (1946). *Boll. Soc. ital. Med. Ig. trop.*, 6, 243.

By inoculating pus from lymphogranuloma venereum anally into lice, following Weigl's technique for infecting lice with rickettsiae, the author claims to have obtained growth of rickettsial forms from the virus of lymphogranuloma venereum.

[Insufficient steps appear to have been taken to exclude infection of the lice with *Rickettsiae* type Rocha Lima, which are common commensals in the intestine of lice in Africa.]

G. M. Findlay

Streptomycin in the Therapy of Granuloma Inguinale. GREENBLATT, R. B., KUPPERMAN, H. S., and DIENST, R. B. (1947). *Proc. Soc. exp. Biol. N.Y.*, 64, 389.

Antimonial preparations are well established in the treatment of granuloma inguinale, but the lesions may recur even if local therapy is also employed. Penicillin seems of little value. Streptomycin has proved so effective in the treatment of 23 cases that the authors consider a preliminary report justified. The condition was diagnosed by the finding of Donovan bodies, either in smears or in biopsy sections. No other drug was used. Doses ranged from 0.3 g. to 1 g. daily; treatment was given every 4 hours and lasted from 6 to 46 days. Healing was usually centripetal, and Donovan bodies could not be demonstrated in smears taken from 5 to 9 days after treatment had started; the moist ulcerated areas around the scrotum took longest to heal, but were ultimately covered by scar tissue.

Toxic reactions occurred in 2 patients after 10 days' treatment. One developed a maculopapular rash on the limbs and lower jaw, with a fine vesicular eruption and oedema of the lips; none of the lesions responded to "benadryl" (100 mg. daily). The other patient complained of a mild burning of the conjunctiva, which did not reappear when the drug was renewed after a short pause.

Relapses may occur, even when as much as 28 g. has been given. In spite of this, streptomycin is undoubtedly the most effective agent known today for treating granuloma inguinale.

T. E. C. Early

PUBLIC HEALTH

Ten Years of Premarital Blood Test Law. TALBOT, H. P. (1947). *Med Offr.*, 77, 55.

This article describes the procedure in obtaining a premarital blood test certificate and tabulates the numerical results of the application of this law in Connecticut. The objectives of the law are: (1) to prevent an individual with syphilis from infecting the marital partner; (2) to prevent congenital syphilis; and (3) to uncover syphilis so that proper treatment may be given. Blood samples can be taken by any licensed physician and sent for test to an approved laboratory. If the result is satisfactory a certificate is signed by the physician and by the applicant in his presence. This is valid for 40 days and must be produced to obtain a marriage licence. The physician does not sign if the applicant is found to have syphilis in a communicable stage. The disease is not usually infectious to the marital partner after 4 or 5 years even in the absence of treatment. A woman with untreated syphilis is always potentially dangerous to her offspring. The rate of positive individuals varied in the 10 years between 9.7 and 19.1 per thousand. A great many were unaware that they were infected, and often the physician was able to sign the certificate as the disease was not in a communicable form.

[The great value of premarital blood tests in unmasking syphilis is well illustrated.]

James Marshall